

RECEIVED

AUG 12 2002

TECH CENTER 1600/2800



1600

1644

## RAW SEQUENCE LISTING

DATE: 08/02/2002

PATENT APPLICATION: US/09/634,287A

TIME: 09:00:02

Input Set : A:\sequence\_DM6909B.txt.txt

Output Set: N:\CRF3\08022002\I634287A.raw

p.6

4 <110> APPLICANT: Bristol-Myers Squibb Company  
 6 <120> TITLE OF INVENTION: AGGRECAN DEGRADING METALLO PROTEASES  
 8 <130> FILE REFERENCE: DM6909B  
 10 <140> CURRENT APPLICATION NUMBER: US/09/634,287A  
 12 <141> CURRENT FILING DATE: 2000-08-09  
 14 <160> NUMBER OF SEQ ID NOS: 21  
 16 <170> SOFTWARE: PatentIn version 3.0  
 18 <210> SEQ ID NO: 1  
 20 <211> LENGTH: 4192  
 22 <212> TYPE: DNA  
 24 <213> ORGANISM: Homo sapiens  
 26 <220> FEATURE:  
 28 <221> NAME/KEY: CDS  
 30 <222> LOCATION: (406)..(2916)  
 32 <400> SEQUENCE: 1  
 33 acagacacat atgcacgaga gagacagagg aggaaagaga cagagacaaa ggcacagcgg 60  
 35 aagaaggcag agacagggca ggcacagaag cggcccagac agagtcctac agagggagag 120  
 37 gccagagaag ctgcagaaga cacaggcagg gagagacaaa gatccaggaa aggagggctc 180  
 39 aggaggagag tttggagaag ccagaccctt gggcacctct cccaagccca aggactaagt 240  
 41 tttctccatt tcctttaacg gtctcagcc cttctgaaaa ctttgctct gaccttgga 300  
 43 ggagtccaag cccccaggct acagagagga gctttccaaa gctagggtgt ggaggacttg 360  
 45 gtgccctaga cggcctcagt ccctcccagc tgcagtacca gtgcc atg tcc cag aca 417  
 46 Met Ser Gln Thr  
 47 1  
 49 ggc tcg cat ccc ggg agg ggc ttg gca ggg cgc tgg ctg tgg gga gcc 465  
 50 Gly Ser His Pro Gly Arg Gly Leu Ala Gly Arg Trp Leu Trp Gly Ala  
 51 5 10 15 20  
 53 caa ccc tgc ctc ctg ctc ccc att gtg ccg ctc tcc tgg ctg gtg tgg 513  
 54 Gln Pro Cys Leu Leu Leu Pro Ile Val Pro Leu Ser Trp Leu Val Trp  
 55 25 30 35  
 57 ctg ctt ctg cta ctg ctg gcc tct ctc ctg ccc tca gcc cgg ctg gcc 561  
 58 Leu Leu Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser Ala Arg Leu Ala  
 59 40 45 50  
 61 agc ccc ctc ccc cgg gag gag gag atc gtg ttt cca gag aag ctc aac 609  
 62 Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro Glu Lys Leu Asn  
 63 55 60 65  
 65 ggc agc gtc ctg cct ggc tcg ggc gcc cct gcc agg ctg ttg tgc cgc 657  
 66 Gly Ser Val Leu Pro Gly Ser Gly Ala Pro Ala Arg Leu Leu Cys Arg  
 67 70 75 80  
 69 ttg cag gcc ttt ggg gag acg ctg cta cta gag ctg gag cag gac tcc 705  
 70 Leu Gln Ala Phe Gly Glu Thr Leu Leu Leu Glu Leu Glu Gln Asp Ser  
 71 85 90 95 100  
 73 ggt gtg cag gtc gag ggg ctg aca gtg cag tac ctg ggc cag gcg cct 753

ENTERED

## RAW SEQUENCE LISTING

DATE: 08/02/2002

PATENT APPLICATION: US/09/634,287A

TIME: 09:00:02

Input Set : A:\sequence DM6909B.txt.txt

Output Set: N:\CRF3\08022002\I634287A.raw

```

74 Gly Val Gln Val Glu Gly Leu Thr Val Gln Tyr Leu Gly Gln Ala Pro
75                               105                               110                               115
77 gag ctg ctg ggt gga gca gag cct ggc acc tac ctg act ggc acc atc      801
78 Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu Thr Gly Thr Ile
79                               120                               125                               130
81 aat gga gat ccg gag tcg gtg gca tct ctg cac tgg gat ggg gga gcc      849
82 Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp Asp Gly Gly Ala
83                               135                               140                               145
85 ctg tta ggc gtg tta caa tat cgg ggg gct gaa ctc cac ctc cag ccc      897
86 Leu Leu Gly Val Leu Gln Tyr Arg Gly Ala Glu Leu His Leu Gln Pro
87                               150                               155                               160
89 ctg gag gga ggc acc cct aac tct gct ggg gga cct ggg gct cac atc      945
90 Leu Glu Gly Gly Thr Pro Asn Ser Ala Gly Gly Pro Gly Ala His Ile
91 165                               170                               175                               180
93 cta cgc cgg aag agt cct gcc agc ggt caa ggt ccc atg tgc aac gtc      993
94 Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro Met Cys Asn Val
95                               185                               190                               195
97 aag gct cct ctt gga agc ccc agc ccc aga ccc cga aga gcc aag cgc      1041
98 Lys Ala Pro Leu Gly Ser Pro Ser Pro Arg Pro Arg Arg Ala Lys Arg
99                               200                               205                               210
101 ttt gct tca ctg agt aga ttt gtg gag aca ctg gtg gtg gca gat gac      1089
102 Phe Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val Val Ala Asp Asp
103                               215                               220                               225
105 aag atg gcc gca ttc cac ggt gcg ggg cta aag cgc tac ctg cta aca      1137
106 Lys Met Ala Ala Phe His Gly Ala Gly Leu Lys Arg Tyr Leu Leu Thr
107                               230                               235                               240
109 gtg atg gca gca gca gcc aag gcc ttc aag cac cca agc atc cgc aat      1185
110 Val Met Ala Ala Ala Ala Lys Ala Phe Lys His Pro Ser Ile Arg Asn
111 245                               250                               255                               260
113 cct gtc agc ttg gtg gtg act cgg cta gtg atc ctg ggg tca ggc gag      1233
114 Pro Val Ser Leu Val Val Thr Arg Leu Val Ile Leu Gly Ser Gly Glu
115                               265                               270                               275
117 gag ggg ccc caa gtg ggg ccc agt gct gcc cag acc ctg cgc agc ttc      1281
118 Glu Gly Pro Gln Val Gly Pro Ser Ala Ala Gln Thr Leu Arg Ser Phe
119                               280                               285                               290
121 tgt gcc tgg cag cgg ggc ctc aac acc cct gag gac tcg gac cct gac      1329
122 Cys Ala Trp Gln Arg Gly Leu Asn Thr Pro Glu Asp Ser Asp Pro Asp
123                               295                               300                               305
125 cac ttt gac aca gcc att ctg ttt acc cgt cag gac ctg tgt gga gtc      1377
126 His Phe Asp Thr Ala Ile Leu Phe Thr Arg Gln Asp Leu Cys Gly Val
127                               310                               315                               320
129 tcc act tgc gac acg ctg ggt atg gct gat gtg ggc acc gtc tgt gac      1425
130 Ser Thr Cys Asp Thr Leu Gly Met Ala Asp Val Gly Thr Val Cys Asp
131 325                               330                               335                               340
133 ccg gct cgg agc tgt gcc att gtg gag gat gat ggg ctc cag tca gcc      1473
134 Pro Ala Arg Ser Cys Ala Ile Val Glu Asp Asp Gly Leu Gln Ser Ala
135                               345                               350                               355
137 ttc act gct gct cat gaa ctg ggt cat gtc ttc aac atg ctc cat gac      1521
138 Phe Thr Ala Ala His Glu Leu Gly His Val Phe Asn Met Leu His Asp

```

## RAW SEQUENCE LISTING

DATE: 08/02/2002

PATENT APPLICATION: US/09/634,287A

TIME: 09:00:02

Input Set : A:\sequence DM6909B.txt.txt

Output Set: N:\CRF3\08022002\I634287A.raw

139		360		365		370		
141	aac tcc aag cca tgc atc agt ttg aat ggg cct ttg agc acc tct cgc							1569
142	Asn Ser Lys Pro Cys Ile Ser Leu Asn Gly Pro Leu Ser Thr Ser Arg							
143		375		380		385		
145	cat gtc atg gcc cct gtg atg gct cat gtg gat cct gag gag ccc tgg							1617
146	His Val Met Ala Pro Val Met Ala His Val Asp Pro Glu Glu Pro Trp							
147		390		395		400		
149	tcc ccc tgc agt gcc cgc ttc atc act gac ttc ctg gac aat ggc tat							1665
150	Ser Pro Cys Ser Ala Arg Phe Ile Thr Asp Phe Leu Asp Asn Gly Tyr							
151	405		410		415		420	
153	ggg cac tgt ctc tta gac aaa cca gag gct cca ttg cat ctg cct gtg							1713
154	Gly His Cys Leu Leu Asp Lys Pro Glu Ala Pro Leu His Leu Pro Val							
155		425		430		435		
157	act ttc cct ggc aag gac tat gat gct gac cgc cag tgc cag ctg acc							1761
158	Thr Phe Pro Gly Lys Asp Tyr Asp Ala Asp Arg Gln Cys Gln Leu Thr							
159		440		445		450		
161	ttc ggg ccc gac tca cgc cat tgt cca cag ctg ccg ccg ccc tgt gct							1809
162	Phe Gly Pro Asp Ser Arg His Cys Pro Gln Leu Pro Pro Pro Cys Ala							
163		455		460		465		
165	gcc ctc tgg tgc tct ggc cac ctc aat ggc cat gcc atg tgc cag acc							1857
166	Ala Leu Trp Cys Ser Gly His Leu Asn Gly His Ala Met Cys Gln Thr							
167		470		475		480		
169	aaa cac tcg ccc tgg gcc gat ggc aca ccc tgc ggg ccc gca cag gcc							1905
170	Lys His Ser Pro Trp Ala Asp Gly Thr Pro Cys Gly Pro Ala Gln Ala							
171	485		490		495		500	
173	tgc atg ggt ggt cgc tgc ctc cac atg gac cag ctc cag gac ttc aat							1953
174	Cys Met Gly Gly Arg Cys Leu His Met Asp Gln Leu Gln Asp Phe Asn							
175		505		510		515		
177	att cca cag gct ggt ggc tgg ggt cct tgg gga cca tgg ggt gac tgc							2001
178	Ile Pro Gln Ala Gly Gly Trp Gly Pro Trp Gly Pro Trp Gly Asp Cys							
179		520		525		530		
181	tct cgg acc tgt ggg ggt ggt gtc cag ttc tcc tcc cga gac tgc acg							2049
182	Ser Arg Thr Cys Gly Gly Gly Val Gln Phe Ser Ser Arg Asp Cys Thr							
183		535		540		545		
185	agg cct gtc ccc cgg aat ggt ggc aag tac tgt gag ggc cgc cgt acc							2097
186	Arg Pro Val Pro Arg Asn Gly Gly Lys Tyr Cys Glu Gly Arg Arg Thr							
187		550		555		560		
189	cgc ttc cgc tcc tgc aac act gag gac tgc cca act ggc tca gcc ctg							2145
190	Arg Phe Arg Ser Cys Asn Thr Glu Asp Cys Pro Thr Gly Ser Ala Leu							
191	565		570		575		580	
193	acc ttc cgc gag gag cag tgt gct gcc tac aac cac cgc acc gac ctc							2193
194	Thr Phe Arg Glu Glu Gln Cys Ala Ala Tyr Asn His Arg Thr Asp Leu							
195		585		590		595		
197	ttc aag agc ttc cca ggg ccc atg gac tgg gtt cct cgc tac aca ggc							2241
198	Phe Lys Ser Phe Pro Gly Pro Met Asp Trp Val Pro Arg Tyr Thr Gly							
199		600		605		610		
201	gtg gcc ccc cag gac cag tgc aaa ctc acc tgc cag gcc cgg gca ctg							2289
202	Val Ala Pro Gln Asp Gln Cys Lys Leu Thr Cys Gln Ala Arg Ala Leu							
203		615		620		625		

## RAW SEQUENCE LISTING

DATE: 08/02/2002

PATENT APPLICATION: US/09/634,287A

TIME: 09:00:02

Input Set : A:\sequence DM6909B.txt.txt

Output Set: N:\CRF3\08022002\I634287A.raw

```

205 ggc tac tac tat gtg ctg gag cca cgg gtg gta gat ggg acc ccc tgt      2337
206 Gly Tyr Tyr Tyr Val Leu Glu Pro Arg Val Val Asp Gly Thr Pro Cys
207      630      635      640
209 tcc ccg gac agc tcc tcg gtc tgt gtc cag ggc cga tgc atc cat gct      2385
210 Ser Pro Asp Ser Ser Val Cys Val Gln Gly Arg Cys Ile His Ala
211 645      650      655      660
213 ggc tgt gat cgc atc att ggc tcc aag aag aag ttt gac aag tgc atg      2433
214 Gly Cys Asp Arg Ile Ile Gly Ser Lys Lys Lys Phe Asp Lys Cys Met
215      665      670      675
217 gtg tgc gga ggg gac ggt tct ggt tgc agc aag cag tca ggc tcc ttc      2481
218 Val Cys Gly Gly Asp Gly Ser Gly Cys Ser Lys Gln Ser Gly Ser Phe
219      680      685      690
221 agg aaa ttc agg tac gga tac aac aat gtg gtc act atc ccc gcg ggg      2529
222 Arg Lys Phe Arg Tyr Gly Tyr Asn Asn Val Val Thr Ile Pro Ala Gly
223      695      700      705
225 gcc acc cac att ctt gtc cgg cag cag gga aac cct ggc cac cgg agc      2577
226 Ala Thr His Ile Leu Val Arg Gln Gln Gly Asn Pro Gly His Arg Ser
227      710      715      720
229 atc tac ttg gcc ctg aag ctg cca gat ggc tcc tat gcc ctc aat ggt      2625
230 Ile Tyr Leu Ala Leu Lys Leu Pro Asp Gly Ser Tyr Ala Leu Asn Gly
231 725      730      735      740
233 gaa tac acg ctg atg ccc tcc ccc aca gat gtg gta ctg cct ggg gca      2673
234 Glu Tyr Thr Leu Met Pro Ser Pro Thr Asp Val Val Leu Pro Gly Ala
235      745      750      755
237 gtc agc ttg cgc tac agc ggg gcc act gca gcc tca gag aca ctg tca      2721
238 Val Ser Leu Arg Tyr Ser Gly Ala Thr Ala Ala Ser Glu Thr Leu Ser
239      760      765      770
241 ggc cat ggg cca ctg gcc cag cct ttg aca ctg caa gtc cta gtg gct      2769
242 Gly His Gly Pro Leu Ala Gln Pro Leu Thr Leu Gln Val Leu Val Ala
243      775      780      785
245 ggc aac ccc cag gac aca cgc ctc cga tac agc ttc ttc gtg ccc cgg      2817
246 Gly Asn Pro Gln Asp Thr Arg Leu Arg Tyr Ser Phe Phe Val Pro Arg
247      790      795      800
249 ccg acc cct tca acg cca cgc ccc act ccc cag gac tgg ctg cac cga      2865
250 Pro Thr Pro Ser Thr Pro Arg Pro Thr Pro Gln Asp Trp Leu His Arg
251 805      810      815      820
253 aga gca cag att ctg gag atc ctt cgg cgg cgc ccc tgg gcg ggc agg      2913
254 Arg Ala Gln Ile Leu Glu Ile Leu Arg Arg Pro Trp Ala Gly Arg
255      825      830      835
257 aaa taacctcaact atcccggtctg ccctttctggtg gcaccggggc ctccggactta      2966
258 Lys
261 gctggggagaa agagagagct tctgttgctg cctcatgcta agactcagtg gggaggggct      3026
263 gtgggcgtga gacctgcccc tcctctctgc cctaatagcgc aggetggccc tgccctggtt      3086
265 tcctgcccctg ggaggcagtg atgggttagt ggatggaagg ggctgacaga cagccctcca      3146
267 tctaaactgc cccctctgcc ctgcgggtca caggagggag ggggaaggca gggagggcct      3206
269 gggccccagt tgtattttatt tagtatttat tcaacttttat ttagcaccag ggaaggggac      3266
271 aaggactagg gtccctgggga acctgacccc tgaccctca tagccctcac cctggggcta      3326
273 ggaaatccag ggtggtggtg ataggtataa gtggtgtgtg tatgcgtgtg tgtgtgtgtg      3386
275 tgaaaatgtg tgtgtgctta tgtatgaggt acaacctgtt ctgctttcct ctccctgaat      3446

```

## RAW SEQUENCE LISTING

DATE: 08/02/2002

PATENT APPLICATION: US/09/634,287A

TIME: 09:00:02

Input Set : A:\sequence DM6909B.txt.txt

Output Set: N:\CRF3\08022002\I634287A.raw

```

277 tttattttttt gggaaaagaa aagtcaaggg taggggtgggc cttcagggag tgaggggatta 3506
279 tcctttttttt tttctttctt tttttctttt tttttttgag acagaatctc gctctgtcgc 3566
281 ccaggctgga gtgcaatggc acaatctcgg ctactgcat cctccgcctc ccgggttcaa 3626
283 gtgattctca tgcctcagcc tcttgagtag ctgggattac aggctcctgc caccacgccc 3686
285 ggctaattttt tgttttgttt tgtttgagga cagagtctcg ctattgtcac cagggctgga 3746
287 atgatttcag ctcaactgcaa ccttcgccac ctgggttcca gcaattctcc tgcctcagcc 3806
289 tcccagtag ctgagattat aggcacctac caccacgccc ggctaatttt tgtattttta 3866
291 gtagagacgg ggtttcacca tgttgccag gctggtctcg aactcctgac cttaggtgat 3926
293 ccactcgct tcatctccca aagtgtcggg attacaggcg tgagccaccg tgcctggcca 3986
295 cgcccaacta atttttgtat ttttagtaga gacagggttt caccatgttg gccaggctgc 4046
297 tcttgaactc ctgacctcag gtaatcgacc tgcctcggcc tcccaaagtg ctgggattac 4106
299 aggtgtgagc caccacgccc ggtacatatt ttttaaattg aattctacta tttatgtgat 4166
301 ccttttgagg tcagacagat gtgggt 4192
303 <210> SEQ ID NO: 2
305 <211> LENGTH: 837
307 <212> TYPE: PRT
309 <213> ORGANISM: Homo sapiens
311 <400> SEQUENCE: 2
313 Met Ser Gln Thr Gly Ser His Pro Gly Arg Gly Leu Ala Gly Arg Trp
314 1 5 10 15
316 Leu Trp Gly Ala Gln Pro Cys Leu Leu Pro Ile Val Pro Leu Ser
317 20 25 30
319 Trp Leu Val Trp Leu Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser
320 35 40 45
322 Ala Arg Leu Ala Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro
323 50 55 60
325 Glu Lys Leu Asn Gly Ser Val Leu Pro Gly Ser Gly Ala Pro Ala Arg
326 65 70 75 80
328 Leu Leu Cys Arg Leu Gln Ala Phe Gly Glu Thr Leu Leu Leu Glu Leu
329 85 90 95
331 Glu Gln Asp Ser Gly Val Gln Val Glu Gly Leu Thr Val Gln Tyr Leu
332 100 105 110
334 Gly Gln Ala Pro Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu
335 115 120 125
337 Thr Gly Thr Ile Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp
338 130 135 140
340 Asp Gly Gly Ala Leu Leu Gly Val Leu Gln Tyr Arg Gly Ala Glu Leu
341 145 150 155 160
343 His Leu Gln Pro Leu Glu Gly Gly Thr Pro Asn Ser Ala Gly Gly Pro
344 165 170 175
346 Gly Ala His Ile Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro
347 180 185 190
349 Met Cys Asn Val Lys Ala Pro Leu Gly Ser Pro Ser Pro Arg Pro Arg
350 195 200 205
352 Arg Ala Lys Arg Phe Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val
353 210 215 220
355 Val Ala Asp Asp Lys Met Ala Ala Phe His Gly Ala Gly Leu Lys Arg
356 225 230 235 240
358 Tyr Leu Leu Thr Val Met Ala Ala Ala Ala Lys Ala Phe Lys His Pro

```

RAW SEQUENCE LISTING ERROR SUMMARY      DATE: 08/02/2002  
PATENT APPLICATION: US/09/634,287A      TIME: 09:00:03

Input Set : A:\sequence DM6909B.txt.txt  
Output Set: N:\CRF3\08022002\I634287A.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:21; Xaa Pos. 12

Invalid <213> Response:

Use of "Artificial" only as "<213> Organism" response is incomplete,  
per 1.823(b) of New Sequence Rules. Valid response is Artificial Sequence.

Seq#:21